

Appl. No.: 10/684,893  
Amdt. dated 02/17/2006  
Reply to Office action of November 17, 2005

Amendments to the Claims:

1. (Original) A crosslinked polymeric structure comprising poly(ethylene glycol) (PEG) polymers in the absence of non-PEG polymers, said PEG polymers crosslinked in the absence of photopolymerization or free-radical polymerization so as to form a solid aggregate and having at least some hydrolytically unstable linkages between said PEG polymers that are hydrolyzable under hydrolysis conditions, said hydrolyzable linkages comprising linkages selected from the group consisting of carboxylate esters, phosphate esters, imines, hydrazones, acetals, orthoesters, and oligonucleotides.
2. (Original) The crosslinked polymeric structure of Claim 1 wherein said hydrolytically unstable linkages are sufficient to cause said crosslinked polymeric structure to degrade by hydrolysis in aqueous solution.
3. (Original) The crosslinked polymeric structure of Claim 1 wherein said structure forms a PEG hydrogel in aqueous solution that is subject to hydrolysis.
4. (Original) The crosslinked polymeric structure of Claim 3 wherein the PEG hydrogel formed therefrom has a rate of hydrolysis that is determined at least in part by the structure of said linkages between said PEG polymers.
5. (Currently Amended) The crosslinked polymeric structure of Claim 4 wherein said linkages comprise one or more methylene groups adjacent in proximity to said hydrolytically unstable linkages sufficient to determine at least in part said rate of hydrolysis of said hydrolytically unstable linkages.
6. (Original) The crosslinked polymeric structure of Claim 5 wherein said hydrolysis rate is decreased as the number of said methylene groups is increased.
7. (Currently Amended) The crosslinked polymeric structure of Claim 1 wherein said hydrolytically unstable linkages comprise linkages selected from the group consisting of

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carboxylate esters[.] and phosphate esters, imines, hydrazones, acetals, orthoesters, and oligonucleotides.

8. (Original) The crosslinked polymeric structure of Claim 7 wherein said hydrolytically unstable carboxylate ester linkages are the reaction product of a PEG alcohol and a PEG carboxylic acid and wherein said hydrolytically unstable phosphate ester linkages are the reaction product of a PEG alcohol and a PEG phosphate.

9. (Original) A drug delivery system comprising a poly(ethylene glycol) hydrogel made from the crosslinked polymeric structure of Claim 1.

10. (Currently Amended) A crosslinked polymeric structure of Claim 1 comprising poly(ethylene glycol)-PEG polymers and having a formula selected from the group consisting of:

$\{R[CH_2-O-PEG-W-PEG-W]_p\}_m$ ,  
 $\{R[CH_2-O-PEG-X-PEG-W-PEG-X]_p\}_{n_1}$ , and  
 $\{R[CH_2-O-PEG-X-R'-W-PEG-W-R'-X]_p\}_{n_2}$

wherein m means "matrix" and indicates that the crosslinked structure is a solid aggregate; p is from about 3 to 10 and indicates the number of arms on the polymers forming said crosslinked structure; R is a central branching moiety suitable for making multiarmed PEGs; R' is a hydrocarbon fragment having from about 1 to 10 carbons; W is a hydrolytically unstable linkage comprising linkages selected from the group consisting of esters, imines, hydrazones, acetals, orthoesters, peptides, and oligonucleotides; and X is a hydrolytically stable linkage comprising linkages selected from the group consisting of amides, urethanes, ureas, amines, and sulfonamides.

11. (Original) The crosslinked polymeric structure of Claim 10 wherein R is a moiety selected from the group consisting of glycerol, glycerol oligomers, pentaerythritol, sorbitol, trimethylolpropane, and di(trimethylolpropane).

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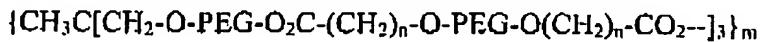
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12. (Original) The crosslinked polymeric structure of Claim 10 wherein said hydrolytically unstable linkages W comprise carboxylate ester linkages that are the reaction product of an alcohol and a carboxylic acid; phosphate ester linkages that are the reaction product of an alcohol and a phosphate; imine linkages that are the reaction product of an amine and an aldehyde; hydrazone linkages that are the reaction product of a hydrazide and an aldehyde; acetal linkages that are the reaction product of an aldehyde and an alcohol; orthoester linkages that are the reaction product of a formate and an alcohol; peptide linkages that comprise linkages selected from the group consisting of peptide linkages that are the reaction product of amines and PEG-peptide conjugates terminated with carboxyl and peptide linkages that are the reaction product of a carboxylic acid and PEG-peptide conjugates terminated with amine; and oligonucleotide linkages that are the reaction product of a phosphoramidite with a 5'-hydroxyl-terminated PEG oligonucleotide.

13. (Original) A drug delivery system comprising a poly(ethylene glycol) hydrogel made from the crosslinked polymeric structure of Claim 10.

14. (Cancelled)

15. (Currently Amended) A crosslinked polymeric structure of Claim 1 comprising poly(ethylene glycol) (PEG) and having the formula:



wherein m means "matrix" and indicates that the crosslinked structure is a solid aggregate, and wherein n is from about 1 to 10.

16. (Withdrawn) The crosslinked polymeric structure of Claim 15 wherein when n equals 2, then the ester linkages have a hydrolysis half life of about 4 days at pH7 and 37 degrees Centigrade, and wherein when n equals 3, then the ester linkages have a hydrolysis half life of about 43 days at pH7 and 37 degrees Centigrade.

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17. (Withdrawn) The crosslinked polymeric structure of Claim 1 wherein said hydrolytically unstable linkages are carboxylate ester linkages.

18. (New) The crosslinked polymeric structure of Claim 17 wherein the carboxylate ester linkage has the structure  $-O-(CH_2)_r-CO_2-$ , wherein r is from about 1 to 10.

19. (New) The crosslinked polymeric structure of Claim 1 wherein said structure further comprises at least one hydrolytically stable linkage selected from the group consisting of amides, urethanes, ureas, amines, and sulfonamides.

20. (New) A crosslinked polymeric structure of Claim 1 having the formula:

$\{R[CH_2-O-PEG-NHCO-(CH_2)_i-O_2C-(CH_2)_n-O-PEG-O-(CH_2)_n-CO_2-(CH_2)_n-CONH-]_p\}_m$   
wherein m means "matrix" and indicates that the crosslinked structure is a solid aggregate, n and i are each from about 1 to 10, and p is from about 3 to 10 and indicates the number of arms on the polymers forming said crosslinked structure.

21. (New) A crosslinked polymeric structure of Claim 1 having the formula:

$\{R[CH_2-O-PEG-NHCO-(CH_2)_n-O-PEG-W-PEG-O-(CH_2)_n-CONH-]_p\}_m$   
wherein m means "matrix" and indicates that the crosslinked structure is a solid aggregate, n is from about 1 to 10, and p is from about 3 to 10 and indicates the number of arms on the polymers forming said crosslinked structure.

22. (New) A crosslinked polymeric structure of Claim 1 having the formula:

$\{R[CH_2-O-PEG-O_2C-(CH_2)_n-O-PEG-O(CH_2)_n-CO_2-]_p\}_m$   
wherein m means "matrix" and indicates that the crosslinked structure is a solid aggregate; p is from about 3 to 10 and indicates the number of arms on the polymers forming said crosslinked structure; R is a central branching moiety selected from the group consisting of glycerol, glycerol oligomers, pentaerythritol, sorbitol, trimethylolpropane, and di(trimethylolpropane); and n is from about 1 to 10.

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23. (New) A crosslinked polymeric structure of Claim 1 further comprising a biologically active substance.

24. (New) A wound dressing comprising a crosslinked polymeric structure of Claim 1.

25. (New) A method for making a crosslinked polymeric structure of Claim 1 comprising reacting a linear poly(ethylene glycol) (PEG) polymer of the formula Z-PEG-Z with a branched PEG polymer of the formula R(CH<sub>2</sub>-O-PEG-Y)<sub>p</sub> to provide a crosslinked structure of the formula {R[CH<sub>2</sub>-O-PEG-W-PEG-W-]\_<sub>p</sub>}<sub>m</sub>, wherein m means "matrix" and indicates that the crosslinked structure is a solid aggregate; p is from 3 to 10 and indicates the number of arms on the polymers forming said crosslinked structure; R is a central branching moiety, Z reacts with Y to form the hydrolytically unstable group W, Z and Y are selected from the group consisting of alcohols, carboxylic acids, amines, aldehydes, hydrazides, phosphates, and formates, and W is selected from the group consisting of carboxylate esters, phosphate esters, imines, hydrazone, acetals, orthoesters, and oligonucleotides.

26. (New) A method of making a crosslinked polymeric structure of Claim 1 comprising reacting a linear poly(ethylene glycol) (PEG) with a branched PEG polymer according to the following equation:

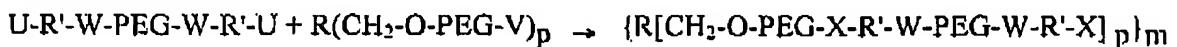
U-PEG-W-PEG-U + R(CH<sub>2</sub>-O-PEG-V)<sub>p</sub> → {R[CH<sub>2</sub>-O-PEG-X-PEG-W-PEG-X-]\_<sub>p</sub>}<sub>m</sub>  
wherein W is selected from the group consisting of esters, imines, hydrazone, acetals, orthoesters, and oligonucleotides; U reacts with V to form X, and U and V are selected from the group consisting of active esters, amines, isocyanates, aldehydes, epoxides, and sulfonate esters; X is selected from the group consisting of amides, urethanes, ureas, amines, and sulfonamides; m means "matrix" and indicates that the crosslinked structure is a solid aggregate; p is from 3 to 10 and indicates the number of arms on the polymers forming said crosslinked structure; and R is a central branching moiety.

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27. (New) A method for making a crosslinked polymeric structure of Claim 1 comprising reacting a linear poly(ethylene glycol) (PEG) with a branched PEG polymer according to the following equation:



wherein R' is a hydrocarbon fragment having from 1 to 10 carbons; W is selected from the group consisting of esters, imines, hydrazones, acetals and orthoesters; U reacts with V to form X; U and V are selected from the group consisting of active esters, amines, isocyanates, aldehydes, epoxides, and sulfonate esters; X is selected from the group consisting of amides, urethanes, ureas, amines, and sulfonamides; m means "matrix" and indicates that the crosslinked structure is a solid aggregate; p is from 3 to 10 and indicates the number of arms on the polymers forming said crosslinked structure; and R is a central branching moiety.